

AMENDMENTS TO THE CLAIMS

WHAT IS CLAIMED IS:

1. (Currently amended) A method of identifying a candidate RB pathway modulating agent, said method comprising the steps of:

- (a) providing an assay system comprising a PSMC 26S protease regulatory subunit C2 (PSMC2) polypeptide or nucleic acid;
- (b) contacting the assay system with a test agent ~~under conditions whereby, but for the presence of the test agent, the system provides a reference activity; and~~
- (c) ~~detecting a test agent-biased~~ determining the activity of the assay system in the presence or absence of the test agent[[,]] ; and
- (d) ~~wherein a difference between the test agent-biased activity and the reference activity identifies~~ identifying the test agent as a candidate RB pathway modulating agent by detecting a difference in the activity of the assay system in the presence or absence of the test agent.

2. (Currently amended) The method of Claim 1_a wherein the assay system comprises cultured cells that express the ~~PSMC~~ PSMC2 polypeptide.

3. (Currently amended) The method of Claim 2_a wherein the cultured cells additionally have defective RB function.

4. (Currently amended) The method of Claim 1_a wherein the assay system includes a screening assay comprising a ~~PSMC~~ PSMC2 polypeptide, and the candidate test agent is a small molecule modulator.

5. (Currently amended) The method of Claim 4_a wherein the assay is an ATPase assay.

6. (Currently amended) The method of Claim 1_a wherein the assay system is selected from the group consisting of an apoptosis assay system, a cell proliferation assay system, an angiogenesis assay system, and a hypoxic induction assay system.

7. (Currently amended) The method of Claim 1_a wherein the assay system includes a binding assay comprising a ~~PSMC~~ PSMC2 polypeptide and the candidate test agent is an antibody.

8. (Currently amended) The method of Claim 1_a wherein the assay system includes an expression assay comprising a ~~PSMC~~ PSMC2 nucleic acid and the candidate test agent is a nucleic acid modulator.

9. (Currently amended) The method of Claim 8_a wherein the nucleic acid modulator is an antisense oligomer.

10. (Currently amended) The method of Claim 8_a wherein the nucleic acid modulator is a phosphothioate morpholino oligomer (PMO).

11. (Currently amended) The method of Claim 1 additionally comprising:
(~~d~~) (e) administering the candidate RB pathway modulating agent identified in (~~e~~) (d) to a model system comprising cells defective in RB function and[[.]] detecting a phenotypic change in the model system that indicates that the RB function is restored.

12.(Currently amended) The method of Claim 11_a wherein the model system is a mouse model with defective RB function.

13. (Withdrawn) A method for modulating a RB pathway of a cell comprising contacting a cell defective in RB function with a candidate modulator that specifically binds to a PSMC polypeptide, whereby RB function is restored.

14. (Withdrawn) The method of Claim 13 wherein the candidate modulator is administered to a vertebrate animal predetermined to have a disease or disorder resulting from a defect in RB function.

15. (Withdrawn) The method of Claim 13 wherein the candidate modulator is selected from the group consisting of an antibody and a small molecule.

16. (Currently amended) The method of Claim 1, comprising the additional steps of:
- (e) providing a ~~secondary~~ second assay system comprising cultured cells or a non-human animal expressing **PSMC PSMC2**, wherein the second assay is capable of detecting a change in the RB pathway;
 - (f) contacting the ~~secondary~~ second assay system with the test agent of (b) or an agent derived therefrom ~~under conditions whereby, but for the presence of the test agent or agent derived therefrom, the system provides a reference activity~~; and
 - (g) detecting ~~an agent-biased activity of a change in~~ a change in the second assay system ~~in the presence or absence of the test agent~~, wherein ~~a difference between the agent-biased activity and the reference activity of~~ change in the second assay system confirms the test agent or agent derived therefrom as a candidate RB pathway modulating agent, ~~and wherein the second assay detects an agent-biased change in the RB pathway~~.
17. (Currently amended) The method of Claim 16, wherein the ~~secondary~~ second assay system comprises cultured cells.
18. (Currently amended) The method of Claim 16, wherein the ~~secondary~~ second assay system comprises a non-human animal.
19. (Currently amended) The method of Claim 18, wherein the non-human animal mis-expresses a RB pathway gene.
20. (Withdrawn) A method of modulating RB pathway in a mammalian cell comprising contacting the cell with an agent that specifically binds a PSMC polypeptide or nucleic acid.
21. (Withdrawn) The method of Claim 20 wherein the agent is administered to a mammalian animal predetermined to have a pathology associated with the RB pathway.
22. (Withdrawn) The method of Claim 20 wherein the agent is a small molecule modulator, a nucleic acid modulator, or an antibody.

23. (Withdrawn) A method for diagnosing a disease in a patient comprising:

- (a) obtaining a biological sample from the patient;
- (b) contacting the sample with a probe for PSMC expression;
- (c) comparing results from step (b) with a control;
- (d) determining whether step (c) indicates a likelihood of disease.

24. (Withdrawn) The method of Claim 23 wherein said disease is cancer.

25. (Withdrawn) The method according to Claim 24, wherein said cancer is a cancer as shown in Table 1 as having >25% expression level.